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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/663,872	09/16/2003	Liliana Tejidor	00825Div.JAR	3114

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EXAMINER	
CHEU, CHANGHWA J	
ART UNIT	**PAPER NUMBER**
1641	

DATE MAILED: 06/20/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/663,872	TEJIDOR ET AL.	
	Examiner	Art Unit	
	Jacob Cheu	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 January 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-100* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-100* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11/15/05; 1/5/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

2. Claims 1, 3-6, 11-14, 17-22, 25-27, 29-32, 36-39, 42-47, 50-51, 87-88, 93-94, are rejected under 35 U.S.C. 102(b) as being anticipated by Hawkins et al. (US 5625036).

With respect to claims 1, 3, 11, 27, 87 and 93-94, Hawkins et al. teach a reagent for use of assessment of hemostatic potential of a blood or plasma sample. Hawkins et al. teach the reagent comprises a coagulation activator, such as recombinant human tissue factor (See Abstract). The recombinant human tissue factor can be from 20 ng/ml which is below the 11 pmolar (Col. 4, line 8-12; Example 1).

With respect to claim 4, 12-13, Hawkins et al. teach using calcium divalent as an ingredient for the reagent (Col. 3, line 25-30).

With respect to claims 5-6, 31-32, Hawkins et al. teach that the reagent is for detecting or assessing hyper, normal or hypo thrombotic state of a patient (See Abstract; Col. 3, line 12-25).

With respect to claim 17, 42, Hawkins et al. teach using stabilizer for the reagent (Col. 3, line 20).

With respect to claims 18-20, 29, 43-45, Hawkins et al. teach using 20 ng/ml to 400 ng/ml recombinant human tissue factor (i.e. molecular weight around 33K-35 K), which is lower than 3 pmolar (Col. 3, line 5-8; Note, See recited Biochemistry 1989, Vol.28, page 8072)

With respect to claims 21-22, 46-47, Hawkins et al. teach using phospholipids at the concentration of 40-250 ng/ml which falls within the range of 10-300 micromolar (Col. 4, line 7-10).

With respect to claims 25-26, 30, 37-38, 50-51, Hawkins et al. teach using 9-15 mM calcium ion which falls within the range of 5-50 mM (Col. 3, line 25-27).

3. Claims 1-8 and 11-15 are rejected under 35 U.S.C. 102(b) as being anticipated by Smirnov et al. (US 5472852).

Smirnov et al. teach an assay for detecting patients of thrombotic disease. Smirnov et al. teach using a coagulant activator, e.g. human tissue factor, allowing assessing of the hemostatic potential of a blood or plasma sample (See claim 35-36).

With respect to claim 2, Smirnov et al. teach using liposome or vesicle for the assay (See Figure 2).

With respect to claims 4, 12-13, Smirnov et al. teach using a divalent ion, i.e. calcium, for the assay (See claim 28).

With respect to claims 7-8, Smirnov et al. teach using phospholipids, including phosphtidylcholine, phosphatidylethanolamine and phosphotidylserine (Col. 3, line 55-62).

4. Claims 1-8, 11-15, 17-22, 25-34, 35-40, 42-47, 50-59, 62-66, 68-73, 76-77, 80, 85-88, 91-94, 97-100 rejected under 35 U.S.C. 102(e) as being anticipated by Brucato et al. (US 6100072).

With respect to claims 1, 27 and 52, Brucato et al. teach a reagent for analyzing thrombotic event in a patient. Brucato et al. teach that the reagent comprises a coagulation activator tissue factor, i.e. rabbit tissue factor where the its ratio to the phospholipids is 0.05 ug per mg phospholipids which falls within the range of less than 11 picomolar, and further the reagent comprise phospholipids vesicle and metal divalent cation, i.e. calcium (Col. 2, line 45; line 65 to Col. 3, line 33).

With respect to the instruction recited in claim 52, such claimed "instructions" is not afforded patentable weight because the recited "instructions" are not functionally related to the underlying kit, but merely teach a new use for an existing product. In re Ngai, 70 USPQ2d 1862 (CAFC 2004).

With respect to claims 2, 7-8, 28, 33-34, 53, 58-59, 85-86, 91-92, 97-98, Brucato et al. teach using different phospholipids vesicle, such as phosphotidylserine and phosphatidylcholine (Col. 3, line 15-18).

With respect to claims 4, 12-13, 25-26, 30, 37-38, 50-51, 55, 63-64, 76-77, Brucato et al. teach using divalent cation, i.e. calcium (about 1-20 mM) for assaying coagulation time of the blood (Col. 3, line 30-45).

With respect to claims 21-22, 46-47, 72-73, the phospholipids used for the assay falls within the range from 10 to 300 micromolar (Col. 3, line 15-25).

With respect to claims 17, 42, 52, Brucato et al. also teach using stabilizer (Col. 3, line 12-13).

With respect to claims 14, 40, 66, the anticoagulant pathway associated with protein C (Col. 7, line 31).

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

7. Claims 9-10, 35, 60-61, are rejected under 35 U.S.C. 103(a) as being unpatentable over Brucato et al. in view of Smirnov et al..

Both Brucato and Smirnov et al. teach using phospholipids, including phosphtidylcholine, phosphatidylethanolamine and phosphotidylserine, to activate tissue

factor for analysis of thrombotic event of blood sample. However, no explicit ratio of phosopholipids are disclosed.

It would have been obvious to one ordinary skill in the art at the time the invention was made to have optimized the ratio of phospholipids for detecting thrombotic assay since it is known that the thromotic assay requires phospholipids for activation of protein C, and discovering the optimum or workable range involves only routine skill in the art. In re Aller, 105 USPQ 233.

8. Claims 16, 23-24, 41, 48-49, 67, 74-75, 78, 81-82, 84, 90, 96 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brucato et al. in view of Broze et al. (Blood 1996 Vol. 88, page 3815-3823).

Brucato et al. reference has been discussed but does not explicitly teach using thromobomodulin, e.g. a protein C activator, for testing coagulation of blood sample.

Broze et al. teach that protein C, a vitamin-K dependence, is of major importance in the control of bleeding involving protein C pathway and teach using thrombomodulin to analyze coagulation of blood sample (See Abstract; page 3821, right column, second paragraph).

Therefore, It would have been obvious to one ordinary skill in the art at the time the invention was made to have provided Brucato et al. with the thrombomodulin as taught by Broze et al. in order to further test blood coagulation via protein C pathway.

With respect to claim 41, 67, Broze et al. teach that the thrombomodulin is a form of soluble human thrombomodulin (See page 3816, right column, third paragraph).

With respect to claims 23-24, 48-49, 74-75, it would have been obvious to one ordinary skill in the art at the time the invention was made to have optimized the amount or

concentration of thrombomodulin for detecting thrombotic assay since it is established when general condition is disclosed in a prior art, discovering the optimum or workable range involves only routine skill in the art. In re Aller, 105 USPQ 233.

With respect to claims 84, 90, 96, it would have been obvious to one ordinary skill in the art at the time the invention was made to have optimize the amount of phosphotidylethanolamine in order to achieve optimal result for the assay because it has been held that when a general condition is disclosed in prior art, discovering the optimum or workable range involves only routine skill in the art. In re Aller, 105 USPQ 233.

9. Claims 79, 83, 95 and 89 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brucato et al. in view of Broze et al, and further in view of Kraus et al. (US 20020019021).

Brucato and Broze et al. references have been discussed but does not explicitly teach using heparin or heparin-like thrombomodulin for analyzing blood coagulation.

Kraus et al. teach the importance of a glycosylated form of thrombomodulin, i.e. heparan sulfate, to the coagulation effect (See Section 0002; Section 0091). Kraus et al also teach using thrombomodulin comprising heparin to analyze blood coagulation. Supra.

Therefore, It would have been obvious to one ordinary skill in the art at the time the invention was made to have provided both Brucato and Broze et al. with the thrombomodulin containing heparin as taught by Kraus et al. in order to further analyze the coagulation effect under various factors, including heparin.

Conclusion

10. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jacob Cheu whose telephone number is 571-272-0814. The examiner can normally be reached on 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Jacob Cheu
Examiner
Art Unit 1641

June 6, 2006

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